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APPELLANTS' BRIEF Address to: Mail Stop Appeal Brief-Patents Commissioner for Patents P.O. Box 1450 Alexandria, VA 22313-1450	Application Number	09/293,670
	Confirmation Number	5176
	Attorney Docket No.	RIGL-036CIP
	Filing Date	April 16, 1999
	First Named Inventor	Joseph Fisher
	Examiner	Teresa D. Wessendorf
	Group Art	1639
	Title: *Multiparameter FACS Assays to Detect Alterations in Cellular Paramters and to Screen Small Molecule Libraries*	

Sir:

This Brief is filed in support of Appellants' appeal from the Examiner's Rejection dated August 10, 2007. No claims have been allowed. Claims 17-36 are pending. Claims 17-26, 30 and 32 are appealed. A Notice of Appeal was filed on November 13, 2007.

The Board of Appeals and Interferences has jurisdiction over this appeal pursuant to 35 U.S.C. §134.

Provided herewith is an authorization to charge the amount of $255.00 to cover the fee required under 37 C.F.R. §41.20(b)(2) for filing Appellants' Brief. In the unlikely event that the fee transmittal or other papers are separated from this document and/or other fees or relief are required, Appellants petition for such relief, including extensions of time, and authorize the Commissioner to charge any fees under 37 C.F.R. §§ 1.16, 1.17 and 1.21 which may be required by this paper, or to credit any overpayment, to deposit account number 50-0815, reference no. RIGL-036 CIP.

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REAL PARTY IN INTEREST

The inventors named on this patent application assigned their entire rights to the invention to Rigel Pharmaceuticals, Inc.

RELATED APPEALS AND INTERFERENCES

There are currently no other appeals or interferences known to Appellants, the undersigned Appellants' representative, or the assignee to whom the inventors assigned their rights in the instant case, which would directly affect or be directly affected by, or have a bearing on the Board's decision in the instant appeal.

STATUS OF CLAIMS

Claims 1-16 were canceled. Claims 17-36 are pending. During the course of prosecution, claims 26-29, 31, 33-36 were withdrawn by the Examiner. Claims 17-26, 30 and 32 are rejected and are appealed herein.

STATUS OF AMENDMENTS

No amendments to the claims were filed subsequent to issuance of the prior Office Action.

SUMMARY OF CLAIMED SUBJECT MATTER

The claimed invention is drawn to a method for screening for an alteration in cellular phenotype. The method includes providing a population of cells comprising a library of retroviral vectors encoding different candidate bioactive agents; sorting the population of cells based on at least five parameters using fluorescence activated cell sorting (FACS); and detecting at least one cell of the population having the alteration in the cellular phenotype. The cellular phenotype is selected from a group of cellular phenotypes consiting of cell cycle, apoptosis, exocytosis, expression of a cell surface receptor, and expression of a receptor protein.

Below is a description of the independent claim and where support for can be

found in the specification.

Independent Claim 17 claims a method of screening for an alteration in cellular phenotype (page 3, line 37 – page 4, line 1). The method includes: a) providing a population of cells comprising a library of retroviral vectors encoding different candidate bioactive agents (page 6, lines 1-11, Fig. 1, and page 19, lines 8-37); b) sorting the population of cells based on at least five parameters using fluorescence activated cell sorting (FACS) (page 4, lines 1-4; and c) detecting at least one cell of the population having the alteration in cellular phenotype (page 15, line 37 – page 16, line 1). The cellular phenotype is selected from a group of cellular phenotypes consisting of cell cycle (page 2, line 11-24), apoptosis (page 11, lines 11-17), exocytosis (page 2, line 26 – page 3, line 33), expression of a cell surface receptor (page 8, line 13), and expression of a receptor protein (page 8, lines 20-24).

GROUNDS OF REJECTION TO BE REVIEWED ON APPEAL

I. Rejection of claims 17-24 and 30 under 35 U.S.C. § 103(a) over Uhr et al. (US 5612185) in view of Conneally et al. (*Blood* 1996, 87: 456-464).

II. Rejection of claims 17-25, 30, and 32 under 35 U.S.C. § 103(a) over Nolan (WO 97/27212), in view of Jia-ping (*Chinese Journal of Physical Medicine* 1995, 17:168-171) and Uhr et al.

III. Rejection of claim 26 under 35 U.S.C. § 103(a) over Nolan, in view of Jia-ping, Uhr et al., Hide et al. (*J. Cell Bio.* 1993, 123:585-593) , and the Appellants' disclosure.

ARGUMENT

I. Claims 17-24 and 30 stand rejected under 35 U.S.C. § 103(a) as being obvious over Uhr et al. in view of Conneally et al.

Claims 17-24 and 30 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Uhr et al. (US 5612185) in view of Conneally et al. (*Blood* 1996

87: 456-464). As best understood by the Appellants, the Examiner believes that Uhr's method for identification of tumor cell types, together with Conneally's teaching of retroviral-mediated gene transfer, renders the claims obvious.

The following arguments are directed to all claims. For the purposes of this appeal, all claims stand or fall together. Claim 17 is representative and set forth below.

> 17. A method of screening for an alteration in cellular phenotype, said method comprising:
>
> a) providing a population of cells comprising a library of retroviral vectors encoding different candidate bioactive agents;
>
> b) sorting said population of cells based on at least five parameters using fluorescence activated cell sorting (FACS); and
>
> c) detecting at least one cell of said population having said alteration in said cellular phenotype;
>
> wherein said cellular phenotype is selected from a group of cellular phenotypes consisting of cell cycle, apoptosis, exocytosis, expression of a cell surface receptor, and expression of a receptor protein.

In a nutshell, the Appellants submit that the claims are not obvious in view of the cited references because neither of the cited references provide a library of retroviral vectors.

As best understood by the Appellants, the Examiner believes that Uhr's method for identifying tumor cell types, in combination with Conneally's method of retroviral-mediated gene transfer, renders the claims obvious.

In order to meet its burden in establishing a rejection under 35 U.S.C. § 103 the Office must first demonstrate that the combined prior art references teach or suggest all the claimed limitations, so as to present

> A finding that the prior art included each element claimed [...] with the only difference between the claimed invention and the prior art being the lack of actual combination...[1]

It is also well established that rejections based on obviousness cannot be sustained by mere conclusory statements; instead, there must be some articulated reasoning to demonstrate that a person of ordinary skill in the art would have been

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1 Federal Register vol. 72, No. 195, Oct 10, 2007. *In re Royka*, 490 F.2d 981, 180 USPQ 580 (CCPA 1974)

prompted to combine elements in the way a claimed invention does. See also e.g., KSR Int'l Co. v. Teleflex Inc., 127 S. Ct. 1727, 1740 (2007):

> "[A] patent composed of several elements is not proved obvious merely by demonstrating that each of its elements was, independently, known in the prior art."[2]

As set forth in the arguments below, the Appellants contend that all cited references are deficient for not teaching or suggesting a method that involves cells comprising a library of retroviral vectors, as required by the rejected claims.

In maintaining this rejection, the Examiner points towards Uhr's column 22, lines 14-20, Fig. 3, and Example 2 and argues that those sections teach a library of retroviral vectors encoding different candidate bioactive agents. However, a detailed analysis of these sections reveals that Uhr does not teach or suggest a population of cells comprising a library of retroviral vectors. When read in context, Uhr, in column 22, teaches that tumor cell cycle arrest may be induced by gene therapy and that a retrovirus may be used to introduce gene constructs. Likewise, Uhr's Fig.3 and Example 2 relate to the expression of oncogenes in tumor cells by assessing mRNA levels of c-myc and c-fos. Hence, these passages are unrelated to cells comprising a library of retroviral vectors.

At no point in Uhr's disclosure, including passages relied upon by the Examiner, does Uhr teach or suggest a library of retroviral vectors.

In attempting to fill the void between Uhr's disclosure and the rejected claims, the Examiner cites Conneally and asserts the Conneally's teaching of retroviral-mediated gene transfer renders the rejected claims obvious. However, Conneally, like Uhr, fails to provide a library of retroviral vectors. Specifically, in the discussion section cited by the Examiner, Conneally teaches that having a cell surface marker such as CD24 encoded by retroviral constructs can facilitate identification and selection of cells. This passage does not provide a library of retroviral vectors, as recited in claim 17.

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[2] See also Pharmastem Therapeutics v. Viacell et al., 2007 U.S. App. LEXIS 16245 (Fed. Cir. 2007);Omegaflex, Inc. v. Parker-Hannifin Corp., 2007 U.S. App. LEXIS 14308 (Fed. Cir. 2007) Dystar Textilfarben GmbH v. C.H. Patrick Co., 464 F.3d 1356, 1360 (Fed. Cir. 2006) In re Kahn, 441 F.3d 977,985 (Fed. Cir. 2006). Medichem, 437 F.3d at 1164. *In re Fulton*, 391 F.3d 1195, 1199-1200 (Fed. Cir. 2004)

For each of the reasons set forth above, Uhr alone or in combination with Conneally does not teach or suggest each and every element of the rejected claims. Since Claim 17 is the only independent claim of this application, the arguments presented above apply with equal force all other rejected claims. Therefore, the Appellants respectfully request the reversal of 103(a) rejections of claims 17-24 and 30 on this basis.

II. Claims 17-25, 30, and 32 are rejected under 35 U.S.C. § 103(a) as being obvious over Nolan, in view of Jia-ping and Uhr et al.

Claims 17-25, 30, and 32 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Nolan et al. (WO 97/27212) in view of Jia et al. (*Chinese Journal of Physical Medicine*), and in further view of Uhr et al. The following arguments are directed to all claims.

The Appellants submit that Nolan cannot preclude the patentability of the rejected claims for the reasons set forth below.

This instant application's earliest priority date is April 17, 1998, as indicated on the filing receipt and the application data sheet of this application. The relevant section of the filing receipt is reproduced below for the Board's convenience.

Domestic Priority data as claimed by applicant

This application is a CIP of 09/157,748 09/21/1998 PAT 6,461,813
which is a CIP of 09/062,330 04/17/1998 PAT 6,897,031

Thus, the instant application claims priority to an application (09/062,330) that was filed on *April 17, 1998*.

Nolan's publication date (July 31, 1997) predates the earliest priority date of this application (April 17, 1997) by less than a year. As such, Nolan only qualifies as prior art only under 35 U.S.C. § 102(a)[3].

A Declaration under 35 U.S.C. § 1.131 (the "Fisher declaration") was

[3] The PCT application upon which Nolan's publication (WO97/27212) is based was filed on January 23, 1997. Nolan's filing date is *prior to* the November 19, 2000 date of enactment of amended 35 U.S.C. § 102(e). As such, Nolan is not available as prior art as of its filing date,

submitted with the Appellants' response dated July 24, 2006, in order to obviate a rejection over a similar combination of references (i.e., Nolan in view of Jai-ping or Ryan). The Fisher Declaration establishes invention of the subject matter of the rejected claims prior to the Nolan's publication date and, as such, Nolan cannot preclude the patentability of the instant claims.

In maintaining this rejection, the Examiner neither discusses the contents of the Fisher Declaration nor provides any evidence that the Applicants did not antedate Nolan's publication date. Rather, the Examiner counters the Appellants' position by simply stating that:

> "Nolan reference was published more than one year of applicants' earliest filing date. Thus, the 35 U.S.C. § 1.131 declaration does not overcome the 103 rejection...."

See page 13 of the Office Action dated August 10, 2007.

As noted above, however, the filing receipt itself states that this application claims priority to an application that was filed on *April 17, 1998.* Since Nolan was published on July 31, 1997, Nolan was published *less than* one year before the Appellants' earliest priority date. As such, the Examiner's position, i.e., that "Nolan was published more than one year of applicants' earliest filing date" lacks support.

In view of the foregoing discussion, the Applicants submit that Nolan is disqualified as a prior art reference and cannot preclude the patentability of the instant claims. Thus, this rejection should be reversed.

III. Claims 26 stands rejected under 35 U.S.C. § 103(a) as being obvious over Nolan, in view of Jia-ping, Uhr et al., Hide et al., and the Appellants' disclosure.

Claim 26 is rejected under 35 U.S.C. § 103(a) as being unpatentable over Nolan et al., in view of Jia et al., Uhr et al. and the Appellants' disclosure. The following arguments are directed to all claims.

As noted in the previous section, the Appellants submit that Nolan cannot be used as prior art under 35 U.S.C. § 103(a) because the subject invention predates

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and is not citable as "102(e)-type art".

the publication date of Nolan.

As such, the Appellants submit that Nolan is disqualified as a prior art reference and cannot preclude the patentability of the instant claims. The Appellants respectfully request the reversal of this rejection.

SUMMARY

I. Claims 17-24 and 30 are not obvious under 35 U.S.C. § 103(a) over Uhr et al. (US 5612185) in view of Conneally et al.

II. Claims 17-25, 30, and 32 are not obvious 35 U.S.C. § 103(a) over Nolan (WO 97/27212), in view of Jia-ping and Uhr et al.

III. Claims 26 is not obvious under 35 U.S.C. § 103(a) over Nolan, in view of Jia-ping, Uhr et al., Hide et al., and the Appellants' disclosure.

RELIEF REQUESTED

The Appellants respectfully request that the rejections of Claims 17-26, 30, and 32 under 35 U.S.C. § 103(a) be reversed, and that the application be remanded to the Examiner with instructions to issue a Notice of Allowance.

Respectfully submitted,

Date: January 28, 2008

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CLAIMS APPENDIX

17. A method of screening for an alteration in cellular phenotype, said method comprising:

a) providing a population of cells comprising a library of retroviral vectors encoding different candidate bioactive agents;

b) sorting said population of cells based on at least five parameters using fluorescence activated cell sorting (FACS); and

c) detecting at least one cell of said population having said alteration in said cellular phenotype;

wherein said cellular phenotype is selected from a group of cellular phenotypes consisting of cell cycle, apoptosis, exocytosis, expression of a cell surface receptor, and expression of a receptor protein.

18. The method according to Claim 17, wherein said candidate agent comprises a fusion partner.

19. The method according to Claim 18, wherein said fusion partner is a fluorescent protein.

20. The method according to Claim 19, wherein said fluorescent protein is a green fluorescent protein (GFP).

21. The method of Claim 17, wherein the cell is a mammalian cell.

22. The method of Claim 21, wherein said mammalian cell is a tumor cell.

23. The method of Claim 21, wherein said mammalian cell is a human cell.

24. The method of Claim 23, wherein said human cell is a human tumor cell.

25. The method of Claim 17, wherein said cellular phenotype is exocytosis.

26. The method of Claim 25, wherein said sorting of said population of cells using fluorescence activated cell sorting (FACS) is based on at least five parameters selected from the group consisting of: light scattering, fluorescent dye update, fluorescent dye release, annexin granule binding, surface granule enzyme activity, and the quantity of granule specific proteins.

30. The method of Claim 17, wherein the candidate bioactive agents are proteins or peptides.

32. The method of Claim 17, further comprising comparing results obtained from said method to results obtained using a positive control, wherein the positive control is p21.

EVIDENCE APPENDIX

No evidence that qualifies under this heading has been submitted during the prosecution of this application, and as such it is left blank.

RELATED PROCEEDINGS APPENDIX

As stated in the *Related Appeals and Interferences* section above, there are no other appeals or interferences known to Appellants, the undersigned Appellants' representative, or the assignee to whom the inventors assigned their rights in the instant case, which would directly affect or be directly affected by, or have a bearing on the Board's decision in the instant appeal. As such this section is left blank.